UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,586	11/30/2000	Michael Kock	49100	5846

26474 7590 09/26/2003

KEIL & WEINKAUF
1350 CONNECTICUT AVENUE, N.W.
WASHINGTON, DC 20036

EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,586	KOCK ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-32* is/are pending in the application.

4a) Of the above claim(s) *5-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of claim 1 and cancellation of claim 4, Paper No. 16, 7/8/2003, is acknowledged. Claims 1-3, 5-32 are still at issue and are present for examination.

Election/Restrictions

Applicants reiteration of their position that the claims as originally filed possess unity of invention as defined in PCT Rule 13 is noted, however applicants are reminded that the previous restriction requirement was deemed proper and made FINAL. Applicants are referred to MPEP Patent Rules:

> **§ 1.144 Petition from requirement for restriction.**
>
> After a final requirement for restriction, the applicant, in addition to making any reply due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested (see § 1.181). [Revised, 62 FR 53131, Oct. 10, 1997, effective Dec. 1, 1997]

Applicants submission that all claims involve or include the presently claimed PARP homolog, which is inventive is not found persuasive as was stated in the previous office actions, the asserted "technical feature" of Group I, even if it is considered a "special technical feature", is not shared by the additional Groups.

Claims 5-32 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 12.

Information Disclosure Statement

Applicants filing of information disclosures, Paper No. 5, filed 1/18/2001, is acknowledged. Those references considered have been initialed. As previously stated, applicants attention is directed to the reference Kupper et al., which does not include the appropriate Journal, Volume and page information. It is requested that this information be added. Applicants statement that this information will be provided as soon as it is available is acknowledged.

Specification

The disclosure is objected to because of the following informalities:

As discussed above, under information disclosure statement, the reference Kupper et al., does not include the appropriate Journal, Volume and Page information. It is requested that this information be added.

Appropriate correction is required.

Claim Objections

Claims 1 remains objected to because of the following informalities:

Claims 1 contain non-elected subject matter (i.e. SEQ ID NO:s 4, 6, 8 and 10).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims **1-3** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection was stated in the previous office action. In response to this rejection, applicants have amended claim 1, cancelled claim 4 and argue the rejection as it applies to the newly amended claims.

Applicants amendment of claim 1 has clarified the claim such that the limitations of a) and b) are understood to be limitations of the claimed "PARP homolog and the functional equivalents thereof".

Applicants further submit that one of skill in the art would find the phrase "functional equivalents" to be sufficiently definite, as the specification discloses various functions of PARP and one of skill in the art would recognize other relevant purposes to which PARP equivalents may be set. As previously stated, a functional polypeptide and thus a "functional equivalent thereof" may encompass a variety of different biological activities. These include but are not limited to immunological activity, such as acting as an antigen for an antibody; regulatory activity, such as that exhibited by many proteins which control transcription and/or translation of not only their encoding nucleic acids but

other nucleic acids as well; or enzymatic activity, for example, polymerase activity. Thus it is unclear what applicants intend to be encompassed by a "functional equivalent thereof" in addition to the structural limitation of 85% homology to SEQ ID NO: 2.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1-4. In response to this rejection, applicants have amended claim 1, cancelled claim 4 and argue the rejection as it applies to the newly amended claims.

Applicants state that the previous examiner's statement that there is no disclosure of structure to function/activity relationship in the specification is not accurate, as applicants state that the instant specification discloses sequences 11-13 (page 4, line 14 to page 5, line 13 of instant specification) to represent a functional NAD+ binding domain and sequence 14 to represent a leucine zipper motif, likely used in dimer formation as well as the disclosure starting on page 5, line 15, through page 6, line 13 which discusses a number of other part-sequence motifs that are preferably present to ensure PARP functionality (See also above 112 2nd paragraph rejection with respect to

"PARP functionality"). Applicants note that the present claims have now been amended to being drawn to those sequences having at least 85% homology with the amino acid sequences specifically claimed and disclosed.

Applicants argument is not found persuasive because as is discussed above there remains some question with respect to what applicants intend in the meaning of "functional equivalents thereof" and further along this line of reasoning, applicants have not defined any function/activity of the claimed "PARP homologs", thus applicants have not disclosed any particular structure to function/activity relationship for the disclosed species as it relates to the claimed genus. The inclusion of such a function/activity limitation combined with applicants structural limitations would help applicants overcome this rejection.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-3 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a poly(ADP-ribose) polymerase (PARP) homolog comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any poly(ADP-ribose) polymerase (PARP) homolog and functional equivalents thereof, comprising a functional NAD^+ binding domain with the sequence $PX_n(S/T)GX_3GKGIYFA$, and lacking any zinc finger motif with the sequence $CX_2CX_MHX_2C$, wherein M is 28 or 30, . The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-4. In response to this rejection, applicants have amended claim 1, cancelled claim 4 and argue the rejection as it applies to the newly amended claims. Applicants in their arguments under 35 USC 112, do not appear to specifically address this rejection based on a lack of scope of enablement, beyond applicants comments above with respect to the disclosure of structure to function/activity relationship under the rejection based on a lack of written description. Thus as stated above, applicants argument as it applies to this rejection is not found persuasive for the reasons stated above and in the previous office action.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims, including all poly (ADP-ribose) polymerases homologs with the specified limitations and functional equivalents thereof. The claims rejected under this section of U.S.C. 112, first paragraph, place minor structural limitations and indefinite if any functional limitations on the claimed molecules. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which

the proteins' structure relates to its function. However, in this case the disclosure is limited to those poly(ADP-ribose) polymerases (PARP) comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8 or 10.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any poly(ADP-ribose) polymerase because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase activity; (B) the general tolerance of poly(ADP-ribose) polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a poly(ADP-ribose) polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the poly(ADP-ribose) polymerase activity claimed and the

fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the allowed number of amino acid modifications of any poly(ADP-ribose) polymerase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

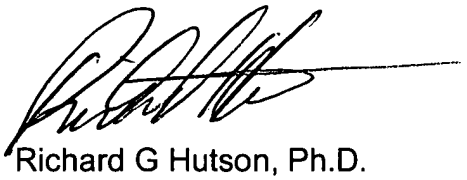
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
9/25/2003